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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :		(11) International Publication Number:	WO 00/13615
A61F 2/28	A1	(43) International Publication Date:	16 March 2000 (16.03.00)

(21) International Application Number: PCT/SE99/01576

(22) International Filing Date: 9 September 1999 (09.09.99)

(30) Priority Data:
9803078-6 9 September 1998 (09.09.98) SE

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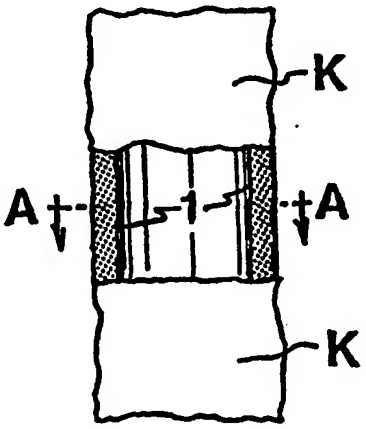
(81) Designated States: AE, AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), DM, EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
In English translation (filed in Swedish).

(54) Title: IMPLANT, METHOD OF MAKING THE SAME AND USE OF THE SAME

(57) Abstract

An implant (prosthesis) comprising a batch of a mixture of porous grains/granular material of tissue-compatible type and disintegrated tissue-compatible biological material (preferably endogenous material, such as bone meal). The batch further comprises a component which allows moulding or modelling of the batch, and the batch is enclosed in a pouch or wrap made of a flexible tissue-compatible material and having pores/apertures/perforations or the like of a size which allows outgrowth and ingrowth of tissue of the biological material. The implant is applicable in many contexts, such as a fixing agent for a hip-bone prosthesis, as a filler in plastic surgery and as a bone growth promoting agent when treating rheumatism.



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IMPLANT, METHOD OF MAKING THE SAME AND USE OF THE SAME

The present invention relates to an implant and a method of making the same and use of the same.

US-A-5,217,496 (Bruce) discloses an implant (prosthesis) comprising a layer of a mixture of pulverulent material of tissue-compatible type and disintegrated tissue-compatible biological material which, by adding a nutrient solution, has been allowed to grow and link the components of the mixture to each other. This patent publication also discloses a method of making such an implant using a mould.

US-A-5,015,256 (Bruce) discloses a means for fixing in a cementless manner a joint prosthesis, comprising a biological compatible granular material of essentially irregular, porous and plastic grains having a size of less than 5 mm. For fixing of the joint prosthesis, the means is inserted into the cavity in which the prosthesis is to be fixed, and the prosthesis is driven into the means and the cavity during vibration of the grains. The vibration causes the grains to be packed in the cavity between prosthesis and cavity wall during interlocking and locking of the prosthesis in the cavity. The mass or bed of the material may contain grains of endogenous material.

Experiments carried out using the above-described fixing technique have proved that a particularly quick and stable, permanent and painless fixing (healing) of prosthesis is achieved precisely if the granular material comprises endogenous material formed of tissue of the same type in/against which the implant is to be inserted or placed, respectively, for instance bone tissue from the femoral cavity if the prosthesis to be fixed is a femoral prosthesis. The bone tissue forms bone (cells) enclosing the grains and extending from the wall

of the cavity to the prosthesis. Moreover, these experiments have shown that the more linked grains of material (plus endogenous material), the quicker fixing of the prosthesis. It seems as if the tendency of the body cells to grow increases the shorter the distance between the grains.

The invention is based on the teachings of the known techniques as described above and of the above-mentioned experiments. The knowledge on which the invention is based thus is that the grains of material must be linked to each other and preferably compacted, and that endogenous biological material, tissue, and nutriment should be available in the material or should have the possibility of penetrating the same.

One could say that the body cavity in US-A-5,015,256 constitutes the mould in the method according to US-A-5,217,496 and comprises natural nutrient solution for cell growth, viz. endogenous body fluid, such as blood.

US-4,755,184 discloses an implant in the form of a sausage, the casing of which consists of a porous hose tied at the ends and containing hydroxyapatite. The casing is firmly packed.

According to the invention, the implant comprises a batch of a mixture of porous grains/granules of tissue-compatible type and of disintegrated tissue-compatible biological material, preferably endogenous tissue and preferably endogenous tissue from the location of the implant, said batch further comprising one more component which makes the batch capable of being moulded or modelled, said batch being enclosed in a pouch or a wrap of a tissue-compatible, flexible sheet, foil, woven fabric, or the like with apertures/perforations/meshes which are permeable for tissue growth from inside the pouch/wrap to the surroundings and from outside into the pouch. The batch must be well kept together and preferably compacted in the pouch/wrap. The latter should be closed, for example sewn together so that no grains/granules can

leave the pouch/wrap. The pouch/wrap may consist of, for instance, gauze bandage.

The preferably performed packing of the batch in the pouch/wrap is carried out to a degree of packing which is necessary for the purpose of the implant. If the purpose of the implant is to support parts of the body or keep a distance between parts of the body, such as vertebrae, the degree of packing must be greater, i.e. be capable of having a supporting and spacing function, than in the case where it is a matter of filling a cavity in the body, such as for plastic surgical purposes, and other purposes if it is a matter of bone growth promoting agent for rheumatics.

The compacting of the batch in the pouch/wrap can advantageously be performed by vibration. Vibration produces the further advantage that the components of the batch are adequately mixed and that nutrient penetrates into the pores of the grains/granules, which is advantageous. Vibration can take place at a certain higher frequency for mixing and another lower frequency for compacting. For vibration, use can be made of e.g. ultrasound.

Nutrient can be added to the batch in vitro, for example by lowering the pouch with the batch into a conventional nutrient solution or blood/plasma and vibrating the pouch, through the wall apertures of which the nutrient reaches the batch to provide tissue growth. However, nutrient can also be added to the batch in vivo, at the location of the implant, which then contains endogenous fluids which can penetrate the pouch.

According to the purpose of application, the implant can be sewn, nailed etc. to the location of the implant in/on the body, which can be necessary when the implant fills a cavity in the body and there is a risk of dislocation. However, if the implant can be expected to be fixed by wedging, such as between vertebrae, no specific fixing means need be used.

The implant is formed during compacting to a shape which well fills the cavity, the space or the distance where it is to be inserted. This is important since otherwise (distance between body tissue and pouch) there is a risk that the implant does not grow on or that connective tissue forms between pouch and body tissue.

It would have become apparent that the shape of the implant according to the invention may be arbitrary, such as a flat plate, a piece of strip, a cylinder, a rod etc.

The pouch containing said mixture can be shaped by using a further/some further tissue-compatible components in the batch which make the batch kneadable and retain the shape of the pouch/wrap caused by the kneading. A suitable component is a hardenable two-component fibrin adhesive which is available on the market, such as from IMMUNO (Schweiz) AG. A further suitable component is FocalSeal (registered trademark), a surgical sealing agent marketed by Focal, Inc. USA. However, it should be emphasised that blood (which contains fibrin and coagulates) in itself is a suitable further component which allows moulding of the mixture in or outside the pouch/wrap to the form of a cavity, to the form of which the implant is to be fitted. As a pattern for the moulding or modelling, use can be made of, for example, an X-ray recording of the body cavity in question.

When considered convenient, the pouch/wrap may be made of a resorbable material. One example is SURGICEL (TM) from ETHICON LTD.

As material for the tissue-compatible grains/granules, it is possible to select according to the invention first of all titanium, but also other materials are suited, which are known to the skilled person for the purpose, such as bioceramics, bioglass, hydroxyapatite, polymers, dextran. Porous grains/granules which are not porous by nature, such as titanium, are obtained in prior-art manner by blowing gas or liquid through a melt of the material.

The grains/granules have an essentially uniform particle size distribution, preferably plastic and irregular. The reason for this is that, when interlocking and compacting by vibration, different particle sizes should not be arranged in layers in the body cavity with the ensuing risk of irregular and thus impaired tissue growth. By an essentially uniform particle size distribution is meant that the grain/granule diameter may vary by ± 50%, preferably by ± 25% or less. The absolute size of the grains/granules may vary in relatively wide ranges, a grain/granule size below 5 mm being considered most convenient. The lower limit may be difficult to establish, and it would be possible to use very small grain particles in combination with a biocompatible liquid which forms the small particles (dust). However, grains/granules above 0.1 mm are normally used. Preferably, the upper limit may be about 2 mm and the lower limit 0.5 mm. It may be generally said that the grain/granule size is selected in consideration of the space which after completed surgery should be packed with grains/granules, i.e. larger grains/granules can be selected for larger body cavities than for small ones. The terms "grains/granules", "irregular" and "diameter" cover other forms than (approximately) spherical.

If the implant according to the invention is to be used for replacement or repair of bone tissue, the grains/granules most preferably consist of plastic or not essentially elastic, continuously porous biocompatible material, preferably metal or metal alloy, such as titanium, having the following porosity characteristics:

- the porosity is continuous
- the opening of pits/indentations/pockets and the channels/passages interconnecting the same has a width of > about 50 μm for bone tissue. Such a porosity results in voids in the grains which are interconnected by channels, passages, so that growth of bone tissue to a part of the outer surface of the grains allows the growth to continue

through individual grains and out through other parts of the outer surface of the grains.

According to the invention, the mixing of the batch components to provide the above-mentioned batch can be carried out before introducing the batches into the pouch or before wrapping the batches. In this connection, a batch of nutrient is added to the mixture. Alternatively, and still according to the invention, the mixing can be carried out after introduction into the pouch or after wrapping the batches.

In, for instance, surgery on the spinal column for replacing worn-out intervertebral discs between vertebrae, use is often made of implants that are screwed between the vertebrae. Such implants are rigid and may contain bone fragments, see US-A-4,501,269 and US-A-5,489,308. Such bone fragments are, however, not available in a sufficient quantity, and it is the implants that have the supporting function and may cause pain. Such implants are also complicated and expensive to manufacture.

The invention remedies this and suggests an implant of the type described above for stabilising the spinal column.

Fig. 1 is a schematic view of two annular-cylindrical pouches 1 having contents as described above and being inserted between two vertebrae K. The pouches 1 are well filled with the batch (the grains/granular material is made of titanium), which has been vibrated for adequate mixing and compacting so that the distance between the vertebrae can be kept correct. Bone forms rapidly and takes over the supporting function. The pouches are made of the above-described, exemplifying resorbable material. Fig. 1a is a sectional view a-a.

Fig. 2 illustrates an implant 2 according to the invention inserted in a hip-bone cavity S for fixing a hip-bone implant 3 in the hip-bone cavity, said hip-bone implant 3 consisting of a conventional plastic cup 4

coated with titanium 5 and resting on, with a press fit, a thin pouch 1 formed according to the hip-bone cavity and containing the above-described batch in which the grains/granules consist of titanium. The pouch 1 is also made of the described, exemplifying resorbable material in the form of a woven fabric.

In one more embodiment of the invention, the interior chamber in a spinal column implant is of the type described in, for instance, US-A-5,015,247 and US-A-4,501,269 filled with an implant according to the invention.

CLAIMS

1. An implant (prosthesis) comprising a batch of a mixture of porous grains/granular material of tissue-compatible type and disintegrated tissue-compatible biological material (preferably endogenous material such as bone meal), characterised in that the batch comprises one more tissue-biocompatible component which allows modelling or moulding of the batch, and that the batch is enclosed in a pouch or wrap made of a flexible tissue-compatible material and having pores/apertures/perforations or the like of a size which allows ingrowth and outgrowth of tissue of the biological material.

2. An implant as claimed in claim 1, characterised in that the flexible material is one of resorbable woven fabric, for instance regenerated cellulose or polymer.

3. An implant as claimed in claim 1 or 2, characterised in that the grains/granular material consists of titanium or polymer or dextran.

4. An implant as claimed in any one of claims 1-3, characterised in that the batch comprises a nutrient/nutrient solution of a kind that promotes growth of the tissue-compatible biological material in the batch.

5. An implant as claimed in any one of claims 1-4, characterised in that the further component is a hardenable component and a hardening agent therefor.

6. An implant as claimed in any one of claims 1-5, characterised in that the further component is blood.

7. An implant as claimed in any one of claims 1-6, characterised in that the size of the grains/granules is between 0.1 and 5 mm, preferably 0.5-2 mm.

8. An implant as claimed in any one of claims 1-7, characterised in that the batch of grains/granules is compacted in the pouch/wrap.

9. An implant as claimed in any one of claims 1-8, characterised in that the grains/granules are plastic or not essentially elastic as well as porous having the following porosity characteristics:

- the porosity is continuous
- the opening of pits/indentations/pockets and the channels/passages interconnecting the same has a width of > about 50 μm for bone tissue.

10. Use of an implant as claimed in any one of claims 1-9 as an intervertebral prosthesis.

11. Use of an implant as claimed in any one of claims 1-9 as a fixing agent for a hip-joint prosthesis.

12. Use of an implant as claimed in any one of claims 1-9 as a filler in, for instance, plastic surgery.

13. Use of an implant as claimed in any one of claims 1-9 as a bone growth promoting agent when treating rheumatism.

14. Use of an implant as claimed in any one of claims 1-9 as filling in body cavities, pits, indentations and the like, or as a carrier between parts of the body, such as between vertebrae.

15. Use of an implant as claimed in any one of claims 1-9 as a spacer in the body.

16. Use of an implant as claimed in any one of claims 1-9 as reinforcement of defective/removed tissue.

17. Use of an implant as claimed in any one of claims 1-9 as tissue (bone) replacement.

18. Use of an implant as claimed in any one of claims 1-9 complementary to conventional implants.

FIG 1

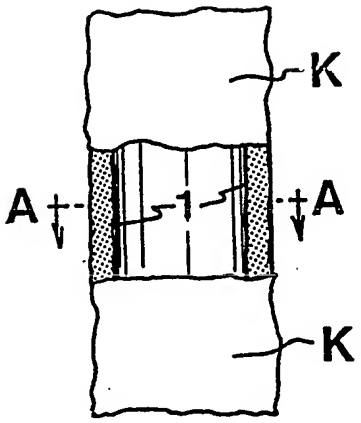


FIG 1a

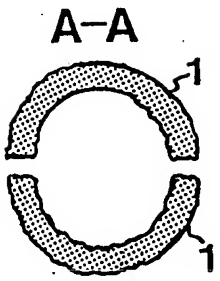
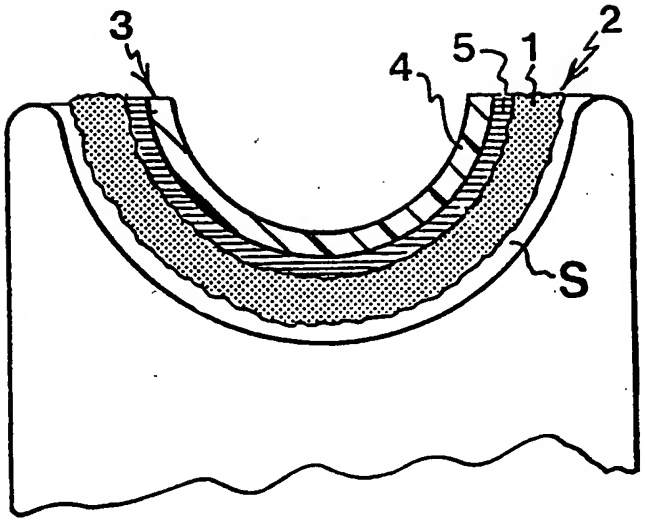


FIG 2



INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 99/01576

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61F 2/28
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61F, A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5217496 A (LARS BRUCE ET AL), 8 June 1993 (08.06.93) --	1-7,9-10,12, 14-16
A	US 4755184 A (MARK SILVERBERG), 5 July 1988 (05.07.88), column 1, line 58 - line 60; column 3, line 37 - line 48 --	1-7,9-10,12, 14-16
A	US 5015256 A (INGRID BRUCE ET AL), 14 May 1991 (14.05.91) --	1-16
A	US 5571189 A (STEPHEN D. KUSLICH), 5 November 1996 (05.11.96) --	1-16

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
10 January 2000	22 -01- 2000
Name and mailing address of the ISA/ Sw dish Patent Offic Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Helena Danielsson/ELY Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 99/01576

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2259252 A (TORAO OHTSUKA), 10 March 1993 (10.03.93), abstract ---	1-16
A	EP 0709070 A2 (OSTEONICS CORP.), 1 May 1996 (01.05.96), column 4, line 24 - line 26, figure 5 --- --------	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE9901576

Box I **Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 10-18
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 10-18 is directed to a method of treatment of the human/animal body, the search has been carried out based on the alleged use of the device.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Box II **Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/SE 99/01576

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Information on patent family members

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